Open Access
J. Food Proc. & Nutr. Res., 2025, 2(2):117-130
ISSN (Online): 3078-9133; ISSN (Print):3078-9125
DOI: https://doi.org/10.22194/ JFPNR /25.1032
https://societyfia.org/journal/JFPNR

Therapeutic Effect of *Salvia Officinalis* against Aberrant Menopause and Its Symptoms: A Comprehensive Review

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A wide range of crippling symptoms, including vasomotor disturbances, psychological changes, and increased long-term metabolic risks are brought on by menopausal transition, which is marked by ovarian decline and variable estrogen levels. The search for non -hormonal alternatives, especially Phyto therapeutics, has increased despite the efficacy of hormone replacement therapy (HRT) and health risks connected with it. The current scientific data focuses on pathophysiological and therapeutic potential of *Salvia officinalis* (common sage), and its efficacy in alleviating menopausal symptoms. A comprehensive review of the literature was done in order to investigate the phytochemical composition and pharmacological effect of *Salvia officinalis*. Phytoestrogens, neuro-active monoterpenes, and strong phenolic antioxidants are only a few of the many bioactive substances found in *Salvia officinalis*. *This* demonstrates significant potential as a safe and effective multi-target therapy for managing menopausal symptoms. However, more rigorous, large-scale clinical trials and standardized extracts are needed to firmly establish its efficacy, optimal dosage, and long-term safety. With further research, sage could emerge as a cornerstone of integrative, non-hormonal menopause management.

Keywords: *Salvia officinalis*, menopause, phytoestrogens, hot flashes, herbal medicine, oxidative stress, neurotransmitter.

INTRODUCTION

Peri menopause is clinically defined as the period between the beginning of irregular menstrual cycles and the definitive cessation of menses (Du et al., 2023). This transition culminates in menopause, a retrospective diagnosis confirmed after 12 consecutive months of amenorrhea, in the absence of other pathological or physiological causes (Duralde et al., 2022). It represents the permanent end of ovarian follicular activity and a woman's reproductive capacity, a process inextricably linked to both ovarian and chronological ageing (Gatenby et al., 2024; Talaulikar et al., 2022).

Ovarian-derived estrogen and progesterone gradually diminish over the perimenopausal era, which can last up to ten years, often commencing in a woman's late 30s or 40s. The mean age of natural menopause is approximately 51 years, though this varies across populations and individuals (Santoro et al., 2021; Kate et al.,2022). This hormonal fluctuation is the primary driver of a constellation of symptoms, including vasomotor symptoms (VMS) like hot flashes and night sweats, psychological disturbances (e.g., anxiety, mood swings), urogenital atrophy, and sleep disturbances, which can severely impair quality of life (QoL) (Poorvi et al.,2024). The subsequent postmenopausal stage brings its own challenges, as the sustained low-estrogen state increases long-term risks for osteoporosis and cardiovascular disease (Proovi et al., 2024; Troia et al.,2021; Vitale et al., 2022).

Hormone replacement therapy (HRT) has been the most successful treatment for relieving menopausal VMS risking some long-lasting disadvantages on health (The NAMS 2022 Hormone Therapy Position Statement Advisory Panel, 2022) (Chen et al., 2023). These limitations have driven interest in plant based remedies. Such as Phyto estrogenic medicinal plants, which contain substances that can have moderate estrogen-like actions are commonly used in these remedies (Patisaul & Jefferson et al., 2010). *Salvia officinalis* (common sage), is a member of the Lamiaceae family, it has long history of traditional use across many countries for treating women's health issues, including excessive sweating and menopausal complaints (Portella et al, 2024). Sage's therapeutic potential may be connected to its diverse

Aziz, F., Amjad, A., Javed, M.S., Zafar, S., Afzal, K., Israr, M. & Javaid, N. (2025). Therapeutic Effect of *Salvia Officinalis* against Aberrant Menopause and Its Symptoms: A Comprehensive Review. *Journal of Food Processing and Nutrition Research*, 2(2), 117-130.
[Received 15 Mar 2025; Accepted 2 May 2025; Published 10 Dec 2025]
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phytochemistry, including flavonoids, phenolic acids, and essential oils (Maggini et al.,2023). It also contributes to reported estrogenic, neuroprotective, and antioxidant activities according to modern scientific research that has started to validate this traditional use (Lopresti et al., 2017; Ghorbani et al., 2017).

Despite promising clinical findings—such as trials demonstrating sage's efficacy in reducing hot flash severity (Bommer et al., 2011; Moradi et al., 2023; Wilfried et al.,2021)—there is a compelling need for a comprehensive and critical synthesis of the current evidence. This review aims to fill that gap by systematically evaluating the therapeutic potential of *Salvia officinalis* against aberrant menopause and its associated symptoms.

The Menopausal Transition: A Pathophysiological Framework

***Endocrinology of Ovarian Aging and Hormonal Fluctuation*:**The irreversible process of ovarian ageing, which is marked by reduction of the pool of primordial follicles, is the primary cause of the menopausal transition. Millions of primordial follicles are present in females at birth, by the time of menopausal transition this number gradually declines, to approximately 1,000 (Sander et al., 2021). Granulosa cells release secretion of anti-Müllerian hormone (AMH) and inhibin B, two important ovarian reserves, critically decreases as a result of this follicular depletion (Hale et al., 2009;). Follicle-stimulating hormone (FSH) levels rise in blood circulating and characteristically when negative feedback on the pituitary gland is lost (Han et al., 2023; Patel P et al., 2025).

Regular ovulary cycles, a marker of reproductive maturity, are typically established one to three years after menarche (Santoro et al., 2021; Wang et al., 2025). The brain, pituitary gland, and ovaries cooperates in highly coordinated manners to support menstrual cycle throughout the reproductive years (Sander et al., 2021). Gonadotropin-releasing hormone (GnRH), which causes the anterior pituitary to release FSH and luteinizing hormone (LH), follicular development and steroidogenesis are regulated by gonadotropin (Grub et l., 2024; Milner et al., 2021). During perimenopause, the axis's normal operation is disturbed (Xiang et al., 2024).

Elevated FSH first causes the remaining antral follicles to recruit and mature more quickly, which can occasionally result to supra-physiological amounts of estradiol (E2) and even episodes of polyvoltine (Brink Vanden et al., 2013; Duralde et al., 2023). As a result, the early perimenopausal period is characterized by vast hormonal fluctuations—oscillating between high E2 and high FSH. Up until five years prior to their last menstrual cycle almost 90% of women are still ovulatory (Corbin et al., 2022). However, anovulatory cycles become more common as the follicular pool approaches exhaustion. Progesterone is not produced during these cycles, and E2 levels fluctuate but eventually declines, resulting in long-lasting hypoestrogenic state of post menopause (Zhao et al., 2025). The effects of aging on GnRH secretion and pituitary responsiveness are linked to a observed variation in LH and FSH after menopause, which shows up as 30-40% drop throughout the transition (Slopien et al., 2020; Kawatika et al., 2023).

The estrogen deprivation has significant clinical ramifications. The onset of perimenopausal mood disorders including depression, anxiety, irritability, and feelings of melancholy is closely linked to variable and lowering E2 levels (De Wit et al., 2021). An individual's sensitivity to these mood swings may be influenced by Genetic polymorphisms in enzymes involved in estrogen metabolism (e.g., CYP1A1) and neurotransmitter regulation (e.g., MAOA, COMT) (Rozycka et al., 2016). Changes in GABA receptor sensitivity, serotonin transporter binding, allopregnanolone (ALLO) levels, neurotrophic factor expression, and systemic inflammation are among the underlying neurobiological mechanisms (Sander et al., 2022).

Global Prevalence and Symptom Burden of Menopause: The experience of menopause, while universal, exhibits significant geographical and demographic variation in its prevalence and symptom presentation. Regional studies provide crucial insight into this burden. For instance, in Pakistan, evidence indicates a high prevalence of perimenopausal symptoms among women aged 45-54, affecting approximately 90% of this demographic (Akbar et al., 2021). A specific study of 100 women found that only 24% reported regular menstrual cycles, while the majority experienced irregularities, with 33% suffering from

Table 1. Hormonal Changes During the Menopausal Transition

Parameter	Reproductive age	Perimenopause		Post menopause
Age	First menstrual cycle -mid-30s	Mid 30-48 years		Remaining life span
Duration		Early	Late	
Menstrual regularity	Normal	Variable length difference of at least 7 days in a row	Amenorrhea Interval of ≥ 60 days	No cycle
Estrogen level	Normal	High/low	High/low	Remains low
FSH level	Normal	High	high	Remain high
Antral follicle count	Normal	Low	Low	Very low

menorrhagia (heavy menstrual bleeding) (Akbar et al., 2021). The vasomotor symptom burden is also considerable; another Pakistani study of 100 women reported that 45% experienced moderate hot flashes and 43% suffered from severe ones (Zulfiqar et al., 2022).

Furthermore, histological findings from endometrial samples of 100 women revealed a high prevalence of pathological changes, with 71% diagnosed with cystic hyperplasia, 19% with adenomatous hyperplasia, and 9.5% with atypical hyperplasia (Munir et al., 2022). This data underscores not only the high frequency of menopausal symptoms but also the significant associated gynecological morbidity in certain populations. The World Health Organization (WHO), citing United Nations population data, estimates that by 2030, the global population of postmenopausal women will exceed 1.2 billion.

***Clinical Spectrum of Menopausal Symptoms*:** Over 80% of women experience the clinical signs of perimenopause, with about one-third having severe and clinically disruptive symptoms (Du et al., 2023; Cunningham et al., 2025). The symptomatology encompasses a wide variety of physiological and psychological changes and goes much beyond the cessation of menses (Zhu et al., 2022).

Vasomotor symptoms (VMS), namely hot flashes and night sweats are most common symptoms (Duralde et al., 2023; Santoro et al., 2021). Sweating, flushing, and palpitations and a sudden intense feeling of heat radiating from the upper body, are common symptoms of hot flashes, which can persist for several minutes (Sander et al., 2021; Oude et al., 2023). These episodes are especially frequent in the late perimenopause and early postmenopausal because estrogen loss interferes with the hypothalamus thermoregulatory center (Santoro et al., 2021; Soumya et al.,2024). VMS has significant negative on sleep quality, causing chronic fatigue, and contributes to mood disturbances and a reduced overall quality of life (McElhany et al., 2024). Most women have these vasomotor symptoms for 1-6 years; however, 10-15% of women will experience severe VMS for 15 years or longer (Du et al., 2023).

The spectrum of symptoms includes:

- **Psychological:** Mood swings, anxiety, irritability, and cognitive issues that are frequently called "brain fog" (Duralde et al., 2023; Sander et al., 2022).
- **Urogenital:** The Genitourinary Syndrome of Menopause (GSM) which include Vaginal dryness, dyspareunia (painful intercourse), and bladder issues such as urgency, frequency, and incontinence (Duralde et al., 2023; Bi Zheng et al., 2025; Waheed et al., 2025). These symptoms are thought to affect 50% of menopausal women, however they are still shockingly underreported (Nik Hazlina et al., 2022).
- **Somatic:** Headaches, heart palpitations are increased during perimenopause (Waliszewska et al., 2025; Gonzaga et al., 2025). Sleep disturbances, chronic fatigue, joint and muscle pain (arthralgia and myalgia) are common problems (Zeng et al., 2025; Duralde et al., 2023; Haufe et al., 2022).
- **Long-Term Risks:** Osteoporosis, cardiovascular disease and neurodegenerative illness are made more likely by persistently low-estrogen state (Santoro et al., 2021), (Weber et al., 2021; Breeze et al., 2024).

***Limitations and Risks of Conventional Therapies*:** The best treatment for reducing menopausal symptoms preventing osteoporosis is still Hormone replacement therapy (HRT) (The NAMS 2022 Therapy Position Statement Advisory Panel, 2022). Hormone as noted by seminal studies like as Women's Health Initiative (WHI) its usage is severely limited by well-known risks such as higher incidence of breast cancer, stroke, and thromboembolic events (Iyer et al., 2024; Zhou et al., 2025). Particularly for women who cannot or choose not to use HRT these worries have increased patient and clinical demand for efficient, non-hormonal, or natural alternatives to manage menopausal symptoms, (Nwaru et al., 2021; Vigneswaran et al., 2022).

Gabapentin, antidepressants for VMS and mood disorders (Pan et al., 2023), are more recent medications as like fezolinetant (Duralde et al., 2022) are examples of alternative pharmaceutical approaches. Non-pharmacological approaches are advised such as dietary recommendations, lifestyle modifications, weight-bearing exercise, and stress management techniques (Chen et al., 2023; Pop et al., 2023). Nonetheless, there is sizable clinical market for evidence-based Phyto therapeutic interventions like *Salvia officinalis* due to continuous search for efficient substitutes with favorable safety profiles (Darabi et al., 2024; Djapardy et al., 2022).

Salvia officinalis: A Plant-based Candidate for Menopause

***Botanical and Phytochemical Profile*:** Salvia officinalis, commonly known as sage, belongs to the family *Lamiaceae* and is widely distributed across Europe, Asia, Africa, and the Americas (Maksimovic et al., 2007; Karalija et al., 2022). It is a perennial shrub reaching ~60 cm in height, characterized by erect, hairy stems, elongated aromatic leaves, and small purplish-blue flowers attractive to pollinators (Boufadi et al., 2021). Taxonomically, it falls under the subfamily *Nepetoideae* and tribe *Mentheae* (Martina et al., 2015).

***Morphological and Edible Parts*:**

- **Leaves**: Used both culinarily and medicinally; rich in flavonoids (luteolin, apigenin, quercetin), phenolic acids (rosmarinic, caffeic, chlorogenic, ferulic), tannins, carnosol, and essential oils. Their bioactivities include hypoglycemic, anti-inflammatory, estrogenic, antioxidant, and immunomodulatory properties (Tayebi et al., 2021; Esmaeili et al., 2022).

- **Flowers**: Bloom from April to June, arranged in spike-like inflorescences of purple, pink, or white shades (Svydenko et al., 2022; Valkovszki et al., 2023).

***Nutritional Profile*:** Sage is a nutrient-dense herb with ~15–25% protein, 26–45% carbohydrates, and 16–33% lipids, contributing ~576 kcal/100g. It contains high levels of glutamic acid, arginine, leucine, and minerals such as iron (1176 µg/g), potassium (23 mg/g), and calcium (Khammar et al., 2021; Uysal et al., 2023).

***Phytochemistry*:** *Salvia officinalis* broad and varied phytochemical profile supports its medicinal potential for menopause (Belcadi et al.,2023). A synergistic combination of several important kinds of bioactive chemicals is responsible for plant's effectiveness (Loukili et al., 2023). It's strong antioxidant and anti-inflammatory properties are mainly due to its abundance of phenolic acids and flavonoids, including rosmarinic acid, luteolin-7-glucoside, apigenin, caffeic acid, chlorogenic acid, rutin, and quercetin (Politi et al., 2022; Jazo et al., 2023). Numerous terpenes and terpenoids such as, α-thujone, β-thujone, camphor, 1,8-cineole, carnosic acid, carnosol, and ursolic acid also contributes its biological action (Svydenko et al., 2022; Mohammadi et al., 2021). Additionally, volatile oils such as borneol, camphene, limonene, α-pinene, and viridiflorol, contributes to its distinctive scent and additional pharmacological properties. Importantly, a major mechanism for the menopausal symptoms is that many of these flavonoids and constituent lignans function as phytoestrogens, work as estrogen receptor modulators (Maggini et al., 2023; Stesevic et al., 2014).

***Safety and Dosage Considerations*:** When taken within therapeutic manners Sage is generally considered as safe. The recommended safe dosage: 300–600 mg/day of dry herb or standardized extract oils, dose higher than this is limited. Sage essential oils contain high thujone and are unsafe to ingest or use because the regulatory assessment and HMPC (EMA) have concluded the health risks of consuming thujone. Thujone is a neurotoxic ketone that can cause restlessness, dizziness, vomiting, tachycardia, seizures, and potential renal damage at high dose, its main cause of toxicity. In contrast standardized extracts (aqueous and ethanolic) with regulated thujone levels used in clinical studies contains minimal thujone and have demonstrated a favorable safety in human trials. Analytical studies using GC-MS found only trace thujone in aqueous extracts and undetectable levels in several commercial standardized preparations.

Mechanisms of Action of Salvia officinalis in Menopause

***Phyto-estrogenic and Hormonal Modulation*:** On the key mechanism by which *Salvia officinalis* alleviates menopausal symptoms is its phyto-estrogenic actions. Vasomotor instability, osteoporosis, genitourinary disease and mood swings are all brought on by the abrupt drop in endogenous estrogen that occurs after menopause (Alrezaki et al.,2021; Bisher et al.,2021). Apigenin, luteolin, and rosmarinic acid are among polyphenolic chemicals that *Salvia officinalis* produce. These compounds share structural similarities with 17 b -estradiol and have ability to bind estrogen receptors (ER-a and ER-b) (Elgayed et al., 2021). These substances are selective estrogen receptor modulators (SERMs), which mimics estrogen-like effects in estrogen-deficient

Table 2. Phytochemical Constituents of *Salvia officinalis* and Their Documented Biological Activities Relevant to Menopause.

Compound/Class	Representative Molecules	Typical Concentration Range	Documented Biological Activity (Relevance to Menopause)	Reference
Phenolic Acids	Rosmarinic acid, caffeic acid, chlorogenic acid, ferulic acid	Rosmarinic: abundant; Caffeic: 1–2%	Strong Antioxidant and anti-inflammatory effects, neuroprotective properties, potential modulation of estrogen pathways	Maggini et al., 2023; mokhtari et al., 2023
Flavonoids	Luteolin, apigenin, quercetin, rutin	Luteolin: ~6.5%; Apigenin: ~25%	Phyto estrogenic activity, anti-anxiety and cognitive enhancing effect, contributes to bone health	Mokhtari et al., 2023
Terpenoids	α-thujone, β-thujone, camphor, 1,8-cineole, carnosic acid, carnosol, ursolic acid	α-thujone: 16–40%; Camphor: 12–35%; 1,8-cineole: 5–22%	Support Vasomotor stability, antimicrobial and anti-inflammatory actions; note: thujone exhibits neurotoxicity at high dose	Stesevic et al., 2014; Silva et al., 2023
Volatile Oils	Borneol, camphene, limonene, α-pinene, viridiflorol	Borneol: 1–10%; Camphene: 2–7%	Aid thermoregulation, exhibits anxiolytic effect, provide cardiovascular support	Durovic et al., 2022; Miroslava et al., 2021
Polyphenols	Ellagic acid, catechins, epicatechin, epigallocatechin gallate	Minor compounds	Potent antioxidant, anti-proliferative activity, supports vascular health	Maggini et al., 2023
Lignans (Phytoestrogens)	Secoisolariciresinol, matairesinol (trace)	Trace levels	Weak estrogen receptor binding activity, potential in alleviating hot flashes in menopause	Maggini et al., 2023

environments without overstimulating the tissues that are estrogen-sensitive.

Additionally, the diterpenes and triterpenoids, of sage can influence the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), to stimulate the hypothalamic-pituitary-gonadal axis, and restore a partial hormonal balance (Sabry et al.,2022; Saleh et al.,2021). Hot flashes, night sweats and vaginal dryness- most of the symptoms of menopause – are directly reduced by this treatment. According to clinical research, women who took a standardized extract of sage reported better subjective well-being and few vasomotor episodes in comparison with placebo groups (Maggini et al.,2023).

***Antioxidant and Anti-inflammatory Pathways*:** There pathophysiology menopause-related problems, including cardiovascular disease, osteoporosis, and cognitive decline is heavily influenced by oxidative stress and systemic inflammation. Menopausal women are more susceptible to chronic illness because of lack of estrogen increases the production of reactive oxygen species (ROS) and amplifies the expression of pro-inflammatory cytokines (Boufadi et al,2021; Mot et al., 2022).

Due to its high concentration polyphenols including rosmarinic acid, caffeic acid, carnosic acid, and carnosol *Salvia officinalis* exhibit great antioxidant activity (Syvdenko et al, 2022; Rahman et al., 2022). Endogenous antioxidant enzymes such as glutathione peroxidase (GPx), catalase (CAT) and superoxide dismutase (SOD) are increased when these bioactive substances activate the Nrf2/ARE signaling pathway. Reduction of DNA damage, lipid peroxidation and mitochondrial malfunction is effective in this molecular defense system (Krisztina Bondar et al., 2025).

Additionally, sage exerts good anti-inflammatory properties via inhibiting nuclear factor kappa B (NF- -κB) and cyclooxygenase-2 (COX-2) and signaling. This results in declined expression of interleukin-6 (IL-6), interleukin-1beta (IL-1 beta) and tumor necrosis factor-alpha (TNF-alpha), which have been shown to mediate vasomotor instability, osteoporosis, and joint pain after menopause (Safi-Eldin et al 2025; Mansour et al., 2023). By preventing oxidative stress and systemic inflammation, all of these mechanisms postpone the development of chronic menopausal comorbidities (Brindisi et al., 2021; Alomar et al., 2023).

***Neuroprotective and Thermoregulatory Effects*:** Anxiety, depression and sleep disturbances and sadness are some of the non-vasomotor menopausal symptoms that have major effect on quality of life significantly and cause cognitive decline (Rhaimi et al., 2023; Faridzadeh et al.,2022). Neurochemical alterations primarily acetylcholine, serotonin and 6-aminobutyric acid (GABA) have been linked with these illnesses. *Salvia officinalis* has neuroprotective benefits it inhibits the enzymes that break down acetylcholine, acetylcholinesterase (AChE) as well as butyryl cholinesterase (BChE). This improves learning, memory, and attention span among postmenopausal women and promotes cholinergic transmissions (Edward et al., 2021)

Additionally, serotonergic and GABAergic receptors react to the sage flavonoids changing neurotransmission to provide anxiolytic and antidepressant effects (Margetts et al., 2022). These procedure aids in reducing menopausal mood disorder and insomnia. sage influences hypothalamic thermoregulatory centers which are highly susceptible to estrogen decline in addition to the neurochemical regulation. Sage reduces hot flashes, night sweats and other vasomotor symptoms by restoring neurotransmitter activity in the hypothalamus (Zeidabadi et al., 2020; Moradi et al., 2023)

Clinical research has verified that *Salvia officinalis* supplementation improves cognition, affectivity, and sleep quality in menopausal women (Wilfried et al., 2021). Sage's Neuroprotective and thermoregulatory properties so create an integrated process that links Phyto activity to symptom relief.

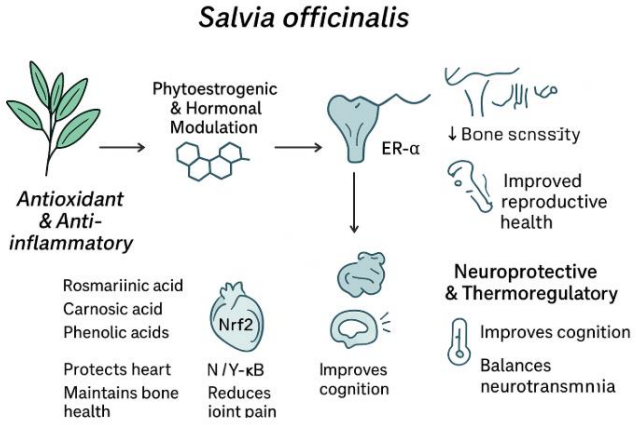

Figure 1. Mechanistic pathways of Phyto-estrogens present in *Salvia officinalis*.

Evidence for Health Benefits and Symptom Alleviation

Effects on Vasomotor Symptoms (Hot Flashes, Sweating)

The most prevalent and bothersome menopausal symptoms hot flashes and night sweats, have been shown to be significantly improved by *Salvia officinalis*. There is current clinical data to support herb's historic use as an anti-sweating agent. According to a study assessing the effectiveness sage extract in managing hot flashes in patients with prostate cancer, both the quantity and frequency of symptoms were considerably reduced (Bommer et al., 2019). It is hypothesized that anti-estrogenic and neuro-modulatory pathways rather than just phyto estrogenic activity are responsible for this effect in order to reduce hot flashes and excessive perspiration (Gatenby et al., 2023). Sage is more successful than a placebo lowering the frequency of hot flashes according to clinical trials (Musial et al., 2021). Furthermore, a specific dried sage extract has been shown to improve not only vasomotor symptoms but also simultaneously have a positive impact on accompanying

somato-vegetative and psychological symptoms, thereby addressing a broad range of menopausal complaints (Tober et al., 2019)

***Benefits for Psychological and Cognitive Health (Mood, Sleep, Memory)*:** Perimenopausal psychological and cognitive issues, including depression, anxiety, mood swings, sleep disorders, and "brain fog," are important targets for *Salvia officinalis* treatment (Corbon et al., 2022; Ertas et al.,2023). Due to its cholinergic qualities, which inhibit acetylcholinesterase (AChE), the dried extract of sage has been shown to significantly improvement in cognitive function in both older and young individuals (Wightman et al.,2021; Metcalf et al., 2023). This enzymatic inhibition is associated with the presence of phenolic acids like rosmarinic acid and monoterpene content (e.g., 1,8-cineole, α-pinene) (Margetts et al., 2022; Edward et al., 2021).

According to quantitative EEG measurements, sage extract affects not only estrogen action but also serotonergic, adrenergic, and GABA-ergic receptors, which are important routes for mood and sleep regulation (Wilfried et al., 2021). Its usage for depression, which worsens during perimenopause; is supported by this multi-targeted mechanism; a randomized clinical trial found that *Salvia officinalis* extract significantly reduced postmenopausal women's depressive symptoms (Tayebi et al., 2021; Lee et al., 2024). The herb's mild adaptogenic properties also help balance cortisol levels, supporting better management of anxiety, irritability, and sleep disturbances (Rhaimi et al., 2023).

***Impact on Metabolic and Long-Term Risks (Obesity, Bone Health, CVD)*:** *Salvia officinalis* exhibit potential in reducing long-term metabolic and health risks concerns linked to estrogen reduction, in addition to basic menopausal symptoms. By reducing serum glucose levels and improving insulin action and production (El euch et al., 2019), the leaves have been used as an anti-diabetic pharmacological drug, demonstrating effectiveness in both Type I and Type II diabetes (Ononamadu et al., 2024; Alharbi et al., 2022). Due to its high amount of flavonoid and phenolic compound content, such as rosmarinic acid sage has substantial benefit against dyslipidemia (Afonso et al., 2021; Abdollahi et al.,2023). These substances have exceptional antioxidant qualities that fights the chronic inflammatory state associated to postmenopausal risks for cardiovascular disease and neurodegenerative disorders (Boufadi et al., 2021; McCarthy et al., 2020). It has been demonstrated that substances such as carnosol and carnosic acid alters inflammatory markers and cytokines, prevents tumor growth by affecting signaling

Table 3. Summary of Clinical Evidence for *Salvia officinalis* in Managing Menopausal Symptoms.

Study Focus	Sample size	Proposed Mechanism	Key Findings	Methodological Critique	Citation
Vasomotor Symptoms	71 women (IIT population = 69)	Binding to GABA/benzodiazepine receptors; central neuro-modulation.	Reduced frequency and severity of hot flashes in menopausal women and prostate cancer patients.	Randomized control trial (RCT); small sample size ;short duration (8 weeks) limited generalizability to diverse populations	Bommer et al.,2019
Vasomotor & Psychological Symptoms	80 years menopausal women (48 - 65yrs)	Multitarget action on neurotransmitter systems (serotonergic, adrenergic, GABAergic).	A specific dried sage extract improved hot flashes, somato-vegetative, and psychological complaints.	RCT design, well-characterized commercial extract ; sample size moderate ; lack of long term follow up ; placebo effects possible	Tober et al 2019; Wilfried et al., 2021
Cognitive Function	Adolescents (n=50) and younger (n=50)	Inhibition of acetylcholinesterase (AChE) by monoterpenes and phenolic acids.	Enhanced cognitive performance in young and older adults.	Double blind ,placebo-controlled ; age groups included both adolescentsAnd adults ;sample size relatively small; single dose acute assessment in some cohort	Edward et al., 2021; Margetts et al., 2022
Depressive Symptoms	Postmenopausal women (n=60)	Modulation of stress response (cortisol) and neurotransmitter systems.	Significant reduction in depressive symptoms in postmenopausal women.	Clinical trials with limited participants ;short interview some preclinical evidence used to support findings ;lack of blinding in certain assesments	Tayebi et al., 2021; Rhaimi et al., 2023
Glycemic Control	Pre-clinical diabetic rats; in silico network pharmacology	Polyphenolic compounds enhance insulin function and glucose metabolism.	Lowered serum glucose levels; improved insulin sensitivity and action in diabetic models.	Preclinical or in silico studies ; findings may not fully translate to humans ; controlled experimental conditions ;no long-term safety data	Ononamadu et al., 2024; Alharbi et al., 2022
Antioxidant & Anti-inflammatory	Pre-clinic / in vitro	High content of phenolic acids, flavonoids and terpenoids; inhibition of ROS production and NF-kB signaling	Demonstrated radical scavenging, reduced ROS, and inhibited NF-κB pathway.	In vitro and animal models; controlled conditions, limited clinical extrapolation; provides mechanistic insight but not direct efficacy in humans	

pathways like NF-κB, and exhibit radical scavenging abilities similar to α-tocopherol (Vitamin E) (Brindisi et al., 2021; Krisztina et al., 2022). There is pronounced rise in low-density- lipoprotein (LDL) and non-high density-lipoprotein (non-HDL) cholesterol levels along with an overall increase in total cholesterol, placing perimenopausal women at an elevated risk for the development of various metabolic disorders (Opoku et al., 2023; Zhong et al., 2025; Iporada et al., 2023). Upon attaining peak bone mass around the age of 30, women generally undergo a gradual decline in bone density of approximately 2% annually (Montoya et al., 2021; Kayalar et al., 2022).

Discussion, Research Gaps, and Future Directions

***Mechanistic Interpretation of Clinical Findings*:** The available data summarize that *Salvia officinalis* L. represents a promising, multi-target Phyto therapeutic substance for treatment of variety of menopausal symptoms (BB Akacha et al., 2024). Sage's medicinal potential is due to potential effects of its varied phytochemical array rather than a single molecule. The reduction of vasomotor symptoms appears to be primarily mediated through central nervous system, the modulation of GABAergic and serotonergic pathways that stabilize hypothalamic thermoregulation, rather than by direct estrogenic activity alone (Wilfried et al., 2021). The antioxidant and anti-inflammatory qualities of its phenolic compounds (rosmarinic acid and carnosic acid), address the underlying oxidative stress and chronic inflammation (Boufadi et al., 2021). It potentially declines long-term risks for cardiovascular disease and osteoporosis (Brindisi et al., 2021; McCarthy & Raval, 2020). Additionally, its monoterpenes acetylcholinesterase inhibitory effect offers molecular explanation of benefits in cognitive function and mood stabilization (Edward et al., 2021; Margetts et al., 2022). This multi-systemic action makes *S. officinalis* a uniquely promising alternative for HRT, targeting both the immediate symptoms and the progressive metabolic outcomes of the menopausal transition.

***Critical Analysis of Limitations in Current Research*:** Despite the compelling traditional use and emerging clinical evidence, the current body of research on *Salvia officinalis* for menopausal symptoms has significant limitations that must be acknowledged.

- ***Methodological Rigor*:** one important drawback is that most of studies that are currently available are either narrowed in scope or lack rigorous methodological design, which make it challenging to reach conclusions. Large, multicenter, randomized controlled trials (RCTs) that asses the herb's effectiveness in variety of populations are hard to come.
- ***Standardization*:** Depending on the plant type, growth conditions, harvest time, and extraction techniques *Salvia officinalis* phytochemical makeup might differ greatly (Tayebi et al, 2021). Consistent preparation and dosing are crucial for ensuring repeatability and clinical adaptability. This lack of standardization makes it difficult to compare outcomes across investigations.
- ***Long-Term Safety*:** Although short-term benefits have been identified and safety profile seems favorable, there is a lack of knowledge about long term safety and efficacy. There is still much to learn about potential side effects, drug interactions, and contraindications, particularly when combined with traditional therapy.
- ***Mechanistic Depth*:** Despite several suggestion, nothing is known at molecular-level about how *Salvia officinalis* precisely modulates menopausal pathways. There is not enough of mechanistic clinical data to completely support its pharmacological claims and a large number of data is still observational or based on traditional use.

***Recommendations for Standardization and Future Studies*:** To translate the potential of *Salvia officinalis* into evidence-based clinical practice, future research must address these gaps with a structured approach:

1. ***High-Quality Clinical Trials*:** large-scale, double-blind, placebo-controlled RCTs with no longer durations should be given priority to conclusively show efficacy, ideal dosage and long-term safety for core menopausal symptoms.
2. ***Standardization*:** The bioactive compounds (e.g., rosmarinic acid, thujones, 1,8-cineole) in their interventions must be meticulously standardize and quantified in future studies. This will allow for the establishment of dose-response relationships and ensure the reliability of clinical outcomes.
3. ***Mechanistic Human Studies*:** Research should include mechanistic endpoints in human trials in addition to observational findings. This could involve monitoring neurotransmitter activity in response to sage supplementation, biomarkers of inflammation (e.g., cytokines) and oxidative stress (e.g., ROS markers).
4. ***Comparative Effectiveness*:** researches directly comparing the efficacy of standardized *S. officinalis* extracts against first-line treatments, such as HRT or SSRIs, would help define its relative position in the menopausal treatment algorithm.
5. ***Focus on Long-Term Health*:** Investigation into the herb's impact on specific long-term menopausal health issues, such as bone mineral density (BMD) loss, lipid profile changes, and cognitive decline, should be a key focus area to validate its protective claims.

Given its promising properties and multi-targeted actions, a concerted research effort could position *Salvia officinalis* as a valuable natural adjunct or alternative in the integrated management of menopause.

CRediT author statement: F. Aziz and A. Amjad designed, prepared the original draft and completed the experiment;

M.S. Javed and S. Zafar prepared the original draft; K. Afzal, M. Israr, and N. Javaid reviewed and finalized the draft.

***Conflict of interest*:** The authors declare no conflict of interest.

***Acknowledgments*:** The authors are very grateful to the supporting staff of the fruits and vegetables processing laboratory.

***Funding*:** No funding available for this research.

***Ethical statement*:** The article does not contain any studies regarding Human and Animal**.**

***Availability of data and material*:** We declare that the submitted manuscript is our original work, which has not been published before and is not currently being considered for publication elsewhere.

***Code availability*:** Not applicable.

***Consent to participate*:** All authors participated in this research study.

***Consent for publication*:** All authors submitted consent to publish this research article in JGIAS.

***Informed consent*:** As the study involves handling of post-harvest fruit and does not include human or animal subjects, formal informed consent is not required.

***SDGs addressed*:** Zero Hunger; Good Health and Well-being; Responsible Consumption and Production.

***Policy referred*:** Women's Health & Menopause Management Policy; Integrative & Herbal Medicine Policy; Research Policy: Evidence-Based Clinical Trials.

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